

REMARKS

In the Office Action dated October 26, 2006, Claims 38 and 42-45 are pending and under examination. Claims 1-37 and 39-41 have been cancelled, without prejudice.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance or at least in better condition for appeal. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 38, 42-43 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Liu et al. (*J. Inorganic Biochemistry* 1998 Vol. 71, page 1-6) in view of Pisanti et al. (*Marine Pollution Bull* (1988) Vol. 19, page 328-333).

The Examiner alleges that Liu et al. teach a method of measuring fluorescence quenching of DNA bound fluorescence dye, e.g. increasing dissociation or inhibition of fluorescent dye bound to the DNA, by a sample containing a metal atom, i.e. copper (II). The Examiner states that Liu et al. teach that the presence of a copper (II) metal would compete with binding the DNA molecule intercalated with the fluorescence ethidium dye. The Examiner asserts that the binding constant of the copper is around 10^{-10} (M⁻¹), which falls within the range of micromolar. The Examiner acknowledges that Liu et al. do not explicitly teach detecting the inhibition or dissociation of the dye on the DNA as an indication of the presence of a metal.

However, the Examiner alleges that Pisanti et al. teach that the presence of metals in the ecosystem, e.g., ocean or rivers, is of great concern because of the potential to impact the quality and physiology of marine organisms. The Examiner contends that Pisanti et al. teach that metal levels, such as copper, are essential for the biological equilibrium of the marine ecosystem.

Therefore, the Examiner alleges that it would have been obvious to one skilled in the art at the time the present invention was made to combine the teachings of Liu et al. and Pisanti et al. to measure the presence of copper in an aquatic sample.

Applicants respectfully submit that under the current case law, to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (emphasis added).

In a recent case, the Federal Circuit further clarifies that the motivation to combine can arise even though there is nothing in the references themselves that suggests that they should be combined. For example, implicit motivation to combine may come from: i) the knowledge generally available to one of ordinary skill in the art; ii) the common general knowledge and established scientific principles; and iii) the universal desire to enhance commercial properties. *Dystar Textilfarben GMBH & Co. Deutschland KG v. C.H. Patrick, Co.*, No. 06-1088 (Fed. Cir. October 03, 2006.)

Applicants respectfully submit that to determine the knowledge generally available to one of ordinary skill in the art, one must establish who is "one of ordinary skill" and what is the pertinent art.

With respect to one of ordinary skill in the art, the law is clear. "The hypothetical 'person having ordinary skill in the art' to which the claimed subject matter pertains would, of necessity have the capability of understanding the scientific and engineering principles applicable to the pertinent art." Ex parte Hiyamizu, 10 USPQ2d 1393, 1394 (Bd. Pat. App. & Inter. 1988). "The Examiner must ascertain what would have been obvious to one of ordinary skill in the art at the time the invention was made, and not to the inventor, a judge, a layman, those skilled in remote arts, or to geniuses in the art at hand. *Environmental Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 218 USPQ 865 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1043 (1984).

Applicants submit that in the present case, the problem to be solved by the present invention is to develop a new method for the detection of heavy metal toxicants in environmental field samples. Therefore, in the present case, one of ordinary skill in the art is an environmental scientist who can detect heavy metal toxicants in environmental samples. The field of endeavor of one of ordinary skill in the art is environmental and/or pollution science. Applicants respectfully submit that an environmental scientist could not reasonably be expected to solve the problem of detecting heavy metals in environmental samples with the complex inorganic chemistry detailed in the article by Liu et al. Applicants submit that an environmental scientist, when searching for prior art, would have been unlikely to identify the article by Liu et al., which is directed to a different field of endeavor. Accordingly, Applicants respectfully submit that the Liu et al. reference is not, "reasonably pertinent to the particular problem" as a matter of law and would not have "logically commended itself to the inventor's attention in considering his problem."

Applicants respectfully submit that in order for an Examiner to rely on a reference under 35 U.S.C. 103, it must be analogous prior art. The Examiner must determine what is 'analogous prior art' for the purpose of analyzing the obviousness of the subject matter at issue. "In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavour or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." See, e.g., *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992); *In re Deminski*, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986); *In re Clay*, 966 F.2d 656, 659, 23 USPQ2d 1058, 1060-61 (Fed. Cir. 1992)) ("A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavour, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem.") (*Wang Laboratories Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767 (Fed. Cir. 1993)).

Applicants respectfully submit that under the current controlling law, the reference to Liu et al. should be considered nonanalogous art. Applicants submit that the Liu et al. reference is a study in inorganic biochemistry, which describes a fluorescence quenching assay and complex mathematical formulae to calculate the binding constants of copper(II) macrocyclic complexes to DNA. It is reasonable to assume that this type of study would not form part of the prior art-base nor form part of the general knowledge of an environmental scientist.

Additionally, with respect to the common general knowledge and established scientific principles, the law provides that "[t]he rationale to modify or combine the prior art does not have to be expressly stated in the prior art; it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal

precedent established by prior case law. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *In re Eli Lilly & Co.*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990); *In re Nilssen*, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988). The rationale supporting an obviousness rejection, may be based on common general knowledge in the art or "well known" prior art. The examiner may take official notice of facts outside of the record which are capable of instant and unquestionable demonstration as being "well known" in the art. *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970) (emphasis added).

Applicants submit that even assuming, *arguendo*, that the Examiner's reasoning has certain logic and scientific basis, that basis alone cannot constitute a ground for a rejection of obviousness under the law. "Although the theoretical mechanism of an invention may be explained by logic and sound scientific reasoning, this fact does not support an obviousness determination unless logic and scientific reasoning would have led one of ordinary skill in the art to make the claimed invention." *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (emphasis added).

Applicants respectfully submit that in the present case, one of ordinary skill in the art (i.e. an environmental scientist) would not have been led to combine the prior art to make the claimed invention as a result of established scientific principles or common general knowledge. Established scientific principles and common general knowledge of an environmental scientist would not include the complex inorganic chemistry of the article by Liu et al. and would not provide any rationale or motivation to combine this reference with the teaching of Pisanti et al.

In view of the above argument, Applicants respectfully submit that the Examiner has unreasonably combined the references and that it was not obvious to one of ordinary skill in the art, at the time the present application was filed, to use nucleic acids as sensing molecules for detecting heavy and/or transitional metal environmental toxicants.

Accordingly, Applicants respectfully submit that under the current controlling law, there can be no explicit or implicit motivation to combine the cited references. The Examiner fails to establish a *prima facie* case of obviousness as a matter of law.

Therefore, the rejection of Claim 38, 42-43 under 35 U.S.C. §103(a) as allegedly unpatentable over Liu et al. in view of Pisanti et al. is overcome and withdrawal thereof is respectfully requested.

Claims 44-45 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Liu et al. in view of Pisanti et al. and further in view of Gold et al. (U.S. Patent No. 6,242,246).

The Examiner acknowledges that both the Liu et al. and Pisanti et al. references are silent in teaching use of solid support for immobilization of DNA for analysis. However, the Examiner alleges that Gold et al. teach an efficient and sensitive screening for DNA binding agents by immobilizing DNA on solid support and measuring the change of dye, e.g., fluorescence, indicative of the presence of the binding agent. The Examiner asserts that Gold et al. teach of variety of choices for solid support, including glass, polystyrene, gold or silicon.

Therefore, the Examiner alleges that it would have been obvious to one skilled in the art at the time the invention was made to combine the teachings of both Liu et al. and Pisanti et al. with that of Gold et al. The Examiner asserts that the solid support for immobilization of DNA for better efficiency is well known for immobilization of molecules on a solid support to increase sensitivity of the assay. The Examiner asserts that the methodology employed by Gold

et al. is in an analogous field, e.g. measuring change of fluoresce dye as indicative of DNA binding agents.

As argued above, Applicants respectfully submit that under the current controlling law, there can be no explicit or implicit motivation to combine the references to Liu et al. and Pisanti et al. Accordingly, a rejection based on the combination of Liu et al. and Pisanti et al. cannot be maintained. The Examiner fails to establish a *prima facie* case of obviousness as a matter of law.

Therefore, the rejection of Claim 44-45 under 35 U.S.C. §103(a) as allegedly unpatentable over Liu et al. in view of Pisanti et al. and further in view of Gold et al. is overcome and withdrawal thereof is respectfully requested.

Thus, in view of the foregoing remarks, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Zhuang Yuan
Registration No. 57,449

Scully, Scott, Murphy & Presser, P.C.
400 Garden City Plaza-Suite 300
Garden City, New York 11530
(516) 742-4343
ZY:ab